

Amendments to the Claims:

The listing of claims presented below reflects the pending claims in the instant application as of the mailing date of the Office Action (*i.e.*, July 16, 2003). No amendments have been made herein to the pending claims, and this listing of claims has been provided solely for the Examiner's convenience.

1. (Once Amended) A spectroscopic method of analyzing a sample, comprising:
irradiating a sample with radiation to produce fluorescence from the sample, wherein the fluorescence is modulated by the sample;
monitoring a first portion of the modulated fluorescence at a first distance from the sample;
monitoring a second portion of the modulated fluorescence at a second distance from the sample, the second distance being different from the first distance; and
comparing the first and second portions of the modulated fluorescence to each other to determine a modulation characteristic of the sample.
2. The method of claim 1, wherein the radiation comprises substantially monochromatic light.
3. The method of claim 1, wherein the radiation comprises laser light.
4. The method of claim 1, wherein irradiating the sample comprises directing radiation at the sample using a waveguide.
5. The method of claim 4, wherein the waveguide is an optical fiber.
6. The method of claim 4, wherein the waveguide is an optical fiber bundle.

7. The method of claim 1, wherein monitoring of the modulated fluorescence comprises:
collecting a portion of the modulated fluorescence; and
determining the intensity of the collected portion of modulated fluorescence.
8. The method of claim 7, wherein the first portion of the modulated fluorescence is collected with a first waveguide and the second portion of the modulated fluorescence is collected with a second waveguide.
9. The method of claim 8, wherein the first waveguide is an optical fiber.
10. The method of claim 8, wherein the first waveguide is an optical fiber bundle.
11. The method of claim 8, wherein the second waveguide is an optical fiber.
12. The method of claim 8, wherein the second waveguide is an optical fiber bundle.
13. The method of claim 1, wherein irradiating the sample comprises directing radiation to the sample using a first waveguide and wherein the fluorescence is monitored using the first waveguide.
14. The method of claim 7, wherein the intensity of the collected portion of the fluorescence is determined with a sensor.
15. The method of claim 7, wherein the intensity of the first portion of the modulated fluorescence is determined with a sensor.
16. The method of claim 7, wherein the intensity of the second portion of the modulated fluorescence is determined with a sensor.

17. The method of claim 7, wherein the intensity of the first portion of the modulated fluorescence is determined with a first sensor and the intensity of the second portion of the modulated fluorescence is determined with a second sensor.
18. The method of claim 7, wherein the first and second portions of the modulated fluorescence are measured consecutively.
19. The method of claim 7, wherein the first and second portions of the modulated fluorescence are measured simultaneously.
20. (Once Amended) The method of claim 1, wherein the method further includes determining the intrinsic fluorescence of the sample.
21. The method of claim 1, wherein the sample is biological material.
22. The method of claim 21, wherein the biological material is living tissue.
23. The method claim of 21, wherein the method further includes determining a physiological property of the biological material using the modulation characteristic.
24. The method of claim 21, wherein the method further includes determining a pathological property of the biological material using the modulation characteristic.
25. The method of claim 22, wherein the method further includes determining a physiological property of the living tissue using the modulation characteristic.
26. The method of claim 25, wherein the physiological property of the tissue is tissue oxygenation.

27. The method of claim 22, wherein the method further includes determining a pathological property of the tissue using the modulation characteristic.
28. The method of claim 27, wherein the pathological property of the tissue is the malignant condition of the tissue.
29. The method of claim 1, wherein either but not both of the distances is substantially zero.
30. A spectroscopic method of analyzing a sample, comprising:
 - irradiating a sample with radiation to produce return radiation from the sample, wherein the return radiation is modulated by the sample;
 - monitoring a first portion of the modulated return radiation at a first distance from the sample;
 - monitoring a second portion of the modulated return radiation at a second distance from the sample;
 - processing the first and second portions of the modulated return radiation to determine a modulation characteristic of the sample,
 - wherein the return radiation is modulated by attenuation.
31. The method of claims 30, wherein the return radiation is attenuated by scattering.
32. The method of claim 30, wherein the return radiation is attenuated by absorption.
33. The method of claim 30, wherein the modulation characteristic of the sample is attenuation.
34. The method of claim 30, wherein the modulation characteristic of the sample is absorption.

35. The method of claim 34, wherein the method further includes determining transmittance.
36. The method of claim 30, wherein the modulation characteristic of the sample is optical rotation.
37. A spectroscopic method of analyzing a sample, comprising:
irradiating a sample with radiation to produce return radiation from the sample, wherein the return radiation is modulated by the sample;
monitoring a first portion of the modulated return radiation at a first distance from the sample;
monitoring a second portion of the modulated return radiation at a second distance from the sample;
processing the first and second portions of the modulated return radiation to determine a modulation characteristic of the sample;
wherein the sample is biological material;
wherein the method further includes determining a physiological property of the tissue using the modulation characteristic; and
wherein the physiological property of the tissue is hypoxia.
38. (Once Amended) A spectroscopic method for determining the oxygenation of a biological material, comprising:
irradiating a sample of a biological material with radiation to produce fluorescence from the sample, wherein the fluorescence is modulated by attenuation of the sample;
monitoring a first portion of the modulated fluorescence at a first distance from the sample;
monitoring a second portion of the modulated fluorescence at a second distance from the sample, the second distance being different from the first distance;
comparing the first and second portions of the modulated fluorescence to each other to determine the attenuation of the sample; and
determining oxygenation of the sample using the attenuation of the sample.

39. A spectroscopic method for determining the oxygenation of a biological material, comprising:

irradiating a sample of a biological material with radiation to produce return radiation from the sample, wherein the return radiation is modulated by attenuation of the sample;

monitoring a first portion of the modulated return radiation at a first distance from the sample;

monitoring a second portion of the modulated return radiation at a second distance from the sample;

processing the first and second portions of the modulated return radiation to determine the attenuation of the sample;

determining oxygenation of the sample using the attenuation of the sample;

wherein the oxygenation of the sample is determined by comparing the attenuation of the sample to the attenuation of a sample having a known level of oxygenation.

40. (Once Amended) A spectroscopic method for determining the concentration of hemoglobin in a biological material, comprising:

irradiating a sample of biological material with radiation to produce fluorescence from the sample, wherein the fluorescence is modulated by attenuation of the sample;

monitoring a first portion of the modulated fluorescence at a first distance from the sample;

monitoring a second portion of the modulated fluorescence at a second distance from the sample, the second distance being different from the first distance;

comparing the first and second portions of the modulated fluorescence to each other to determine the attenuation of the sample; and

determining the concentration of hemoglobin in the sample using the attenuation of the sample.

41. A spectroscopic method for determining the concentration of hemoglobin in a biological material, comprising:

irradiating a sample of a biological material with radiation to produce return radiation

from the sample, wherein the return radiation is modulated by attenuation of the sample;
monitoring a first portion of the modulated return radiation at a first distance from the sample;
monitoring a second portion of the modulated return radiation at a second distance from the sample;
determining the concentration hemoglobin in the sample using the attenuation of the sample;
wherein the concentration of hemoglobin is determined by comparing the attenuation of the sample to the attenuation of a sample having a known concentration of hemoglobin.

42. (Once Amended) A method for determining a physiological characteristic of a biological material, comprising:

irradiating a sample of biological material with radiation to produce fluorescence from the sample, wherein the fluorescence is modulated by the sample;
monitoring a first portion of the modulated fluorescence at a first distance from the sample;
monitoring a second portion of the modulated fluorescence at a second distance from the sample, the second distance being different from the first distance; and
comparing the first and second portions of the modulated fluorescence to each other, using a predictive model, to determine a physiological characteristic of the sample.

43. A method for determining a physiological characteristic of a biological material, comprising:

irradiating a sample of a biological material with radiation to produce return radiation from the sample, wherein the return radiation is modulated by the sample;
monitoring a first portion of the modulated return radiation at a first distance from the sample;
monitoring a second portion of the modulated return radiation at a second distance from the sample;
processing the first and second portions of the modulated return radiation, using a

predictive model, to determine a physiological characteristic of the sample;
wherein the predictive model is a multivariate linear regression.

44. (Once Amended) A method for determining a physiological characteristic of biological material, comprising:

irradiating a sample of biological material with radiation to produce fluorescence from the sample, wherein the fluorescence is modulated by the sample;

monitoring a first portion of the modulated fluorescence at a first distance from the sample;

monitoring a second portion of the modulated fluorescence at a second distance from the sample, the second distance being different from the first distance;

comparing the first and second portions of the modulated fluorescence to each other to determine a modulation characteristic of the sample; and

processing the modulation characteristic using a predictive model to determine a physiological characteristic of the sample.

45. A method for determining a physiological characteristic of a biological material, comprising:

irradiating a sample of a biological material with radiation to produce return radiation from the sample, wherein the return radiation is modulated by the sample;

monitoring a first portion of the modulated return radiation at a first distance from the sample;

monitoring a second portion of the modulated return radiation at a second distance from the sample;

processing the first and second portions of the modulated return radiation, using a predictive model, to determine a physiological characteristic of the sample;

wherein the predictive model is a multicriteria associative memory classifier.

46. (Once Amended) Apparatus for analyzing a sample, comprising:

a source adapted to emit radiation that is directed at a sample to produce fluorescence

from the sample, wherein the fluorescence is modulated by the sample;

a first sensor adapted to monitor the fluorescence at a first distance from the sample and generate a first signal indicative of the intensity of the fluorescence;

a second sensor adapted to monitor the fluorescence at a second distance from the sample and generate a second signal indicative of the intensity of the fluorescence, the second distance being different from the first distance; and

a processor associated with the first sensor and the second sensor and adapted to compare the first and second signals to each other to determine a modulation characteristic of the sample.

47. The apparatus of claim 46, wherein fiber optics transmit the fluorescence to the sensors.

48. (Once Amended) Apparatus for analyzing a sample, comprising:

a source adapted to emit radiation that is directed at a sample volume in a sample to produce fluorescence from the sample, such fluorescence including modulated fluorescence resulting from modulation by the sample;

a first sensor adapted to monitor the fluorescence at a first distance from the sample volume and generate a first signal indicative of the intensity of the fluorescence;

a second sensor adapted to monitor the fluorescence at a second distance from the sample volume and generate a second signal indicative of the intensity of the fluorescence, the second distance being different from the first distance; and

a processor associated with the first sensor and the second sensor and adapted to compare the first and second signals to each other to determine a modulation characteristic of the sample.

49. (Once Amended) Apparatus for determining a modulation characteristic of a biological material, comprising:

a source adapted to emit excitation light;

a first waveguide disposed a first distance from the sample adapted to transmit the excitation light from the light source to the biological material to cause the biological material to produce fluorescence and adapted to collect a first portion of the fluorescence;

a first sensor, associated with the first waveguide, adapted to measure the intensity of the

first portion of the fluorescence and generate a first signal indicative of the intensity of the first portion of the fluorescence;

a second waveguide disposed at a second distance from the sample adapted to collect a second portion of the fluorescence, the second distance being different from the first distance;

a second sensor, associated with the second waveguide, adapted to measure the intensity of the second portion of the fluorescence and generate a second signal indicative of the intensity of the second portion of the fluorescence; and

a processor adapted to compare the first and second signals to each other to determine a modulation characteristic of the biological material.

50. (Once Amended) Apparatus for analyzing a sample, comprising:

a source adapted to emit radiation that is directed at a sample volume in a sample to produce fluorescence from the sample, such fluorescence including modulated fluorescence resulting from modulation by the sample;

a first sensor, displaced by a first distance from the sample volume adapted to monitor the fluorescence and generate a first signal indicative of the intensity of the fluorescence;

a second sensor, displaced by a second distance from the sample volume adapted to monitor the fluorescence and generate a second signal indicative of the intensity of fluorescence, the second distance being different from the first distance; and

a processor associated with the first sensor and the second sensor and adapted to compare the first and second signals to each other to determine a physiological property of the sample.

51. (Once Amended) Apparatus for determining a physiological property of a biological material, comprising:

a source adapted to emit excitation light;

a first waveguide disposed a first distance from the sample, and adapted to transmit the excitation light from the light source to the biological material to cause the biological material to produce fluorescence and further adapted to collect a first portion of the fluorescence;

a first sensor, associated with the first waveguide, for measuring the intensity of the first portion of the fluorescence and generating a first signal representative of the intensity of the first

portion;

a second waveguide disposed at a second distance from the sample, and adapted to collect a second portion of the fluorescence, the second distance being different from the first distance;

a second sensor, associated with the first waveguide, for measuring the intensity of the second portion of the fluorescence and generating a second signal representative of the intensity of the second portion; and

a processor adapted to compare the first and second signals to each other to determine a physiological property of the biological material.

52. (Once Amended) A spectroscopic method of analyzing a sample, comprising:
- irradiating a sample with radiation to produce fluorescence from the sample, wherein the fluorescence is modulated by the sample;
 - monitoring a first portion of the modulated fluorescence at a first distance from the sample;
 - monitoring a second portion of the modulated fluorescence at a second distance from the sample, the second distance being different from the first distance;
 - comparing the first and second portions of the modulated fluorescence to each other to determine a modulation characteristic of the sample;
 - wherein the sample is a biological tissue;
 - wherein the method further includes determining a physiological property of the tissue using the modulation characteristic; and
 - wherein the physiological property of the tissue is ischemia.

53. (Once Amended) A method for determining a physiological characteristic of a biological material, comprising:
- irradiating a sample of a biological material with radiation to produce fluorescence from the sample, wherein the fluorescence is modulated by the sample;
 - monitoring a first portion of the modulated fluorescence at a first distance from the sample;

monitoring a second portion of the modulated fluorescence at a second distance from the sample, the second distance being different from the first distance; and

comparing the first and second portions of the modulated fluorescence to each other, using a predictive model, to determine a physiological characteristic of the sample, wherein the predictive model is multivariate.

54. (Once Amended) A spectroscopic method of analyzing a sample, comprising:
irradiating a sample with radiation to produce fluorescence from the sample, wherein the fluorescence is modulated by the sample;

monitoring a first portion of the modulated fluorescence at a first angle from the sample;

monitoring a second portion of the modulated fluorescence at a second angle from the sample; and

comparing the first and second portions of the modulated fluorescence to each other to determine a modulation characteristic of the sample.